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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER
ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
1631	9

DATE MAILED: 02/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/839,186	MEYERSON, MATTHEW L.	
	Examiner	Art Unit	
	Marianne P. Allen	1631	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26,29-31 and 50-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,19-22 and 50-61* is/are rejected.

7)☒ Claim(s) *10-18,23-26 and 29-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant elected Group I with traverse, substantively amended claim 8 to be within the election of Group I, and cancelled claims 27-28 and 32-49 in Paper No. 8. Claims 1-26, 29-31, and 50-61 are under consideration by the examiner.

Specification

Claims 10-18, 23-26, and 29-31 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. Claim 8 is a multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

Claims 1-9, 19-22, and 50-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

Claims 1, 2, and 3 are directed to methods of using a computer system to identify a microbe inhabiting a host organism. The final step in each claim recites "wherein absence...indicates that said at least one sequence is a candidate sequence belonging to a microbe." The method steps as recited to do not provide the information required by the goal of the preamble. The identification of a candidate sequence does not mean that the sequence is in fact from a microbe nor does it identify what microbe it might be. In each case, the steps only

indicate that at least one sequence is not present in the database of the host organism genomic sequences.

Likewise, the method steps of claim 50 do not identify a microbe inhabiting a host organism as required by the preamble. The steps only identify a plurality of expressed sequences not present in a database of host organism genomic sequences.

The method steps of claim 58 do not identify a microbe inhabiting host organism as required by the preamble. The steps only identify the presence of an expressed sequence in common with at least one non-microbial host organism. This would include, for example, repeat elements.

The specification discloses identification of foreign gene sequences by transcript filtering against a variety of databases containing known and identified (at least as to source) sequences. An EST library from HeLa cervical carcinoma cells which are known to harbor human papilloma virus (HPV) were filtered by comparing sequences between this EST library and matching sequences (matching as defined by algorithmic criteria) from reference human RNA sequences; mitochondrial, vector and repeat element sequences; human genome sequences, and mouse genome sequences. Each filter removed a number of sequences leaving twenty-two non-matching sequences. Twenty of these were eliminated following PCR analysis leaving two HPV sequences already known to be involved in cervical carcinoma. Note that the critical features set forth in the specification filtering multiple times against databases known for their completeness (or presumed completeness such as the human and mouse genome databases) or against databases with known characteristics (such as repeated sequences) are not present in the claims.

Note that the claims have no limitations as to how presence or absence of a sequence is determined. That is, the specification discloses particular algorithms and cut-offs to define presence and absence whereas the claims taken on their face would seem to require exact matching for presence or absence. As such, if the sequence obtained in (a) was longer than a sequence in (b), it would not be considered to be present. Likewise, a sequence reflecting a strain difference would not be considered to be present.

The specification does not provide databases containing expressed sequence tags (ESTs) or genomic sequences for all host organisms embraced by the claims. While the specification indicates that many such databases are available, there is no evidence that these databases possess the type of sequence integrity (produced from host organisms not having a particular pathogenic condition, see for example claim 8) required by the claims. For example, with respect to claim 2, genome databases for host organisms with known symbiotic organisms would reasonably be expected to contain at least some of the symbiotic sequences. The Relman reference acknowledges that microbial and viral transcripts will be present in what are ostensibly human EST databases. (See abstract as well as page 29 of the instant specification.) The specification also acknowledge that microbe sequences can be present due to contamination in preparing libraries or sequences rather than actually being presence in the host organism. For example, with respect to claim 58, databases of microbial sequences would not appear to have been available for many microbes encompassed by the claims. (See page 9, lines 13-20.) ~~specification itself acknowledges that known databases ostensibly~~

Claims 1, 3, and 50 recite "obtaining sequence information...from at least one host organism." If sequence information is obtained from both a human organism and Drosophila

organism, none of the steps recited results in discrimination or assignment of any absent sequence from one or the other host organism or identification of a microbe inhabiting either one.

Claims 4-6, 19-22, 51-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-6 recite limitations with respect to microbes. It appears that what was intended was to limit the claim as to the particular type of microbe found; however, the method steps of the claims provide no steps directed to identifying these particular organisms. As such, the claims are either not further limiting or just confusing.

Claim 19 is confusing in reciting limitations with respect to an "expressed sequence." This claim depends upon claim 8 which in turn depends upon claims 1, 2, or 3. Claim 8 does not recite expressed sequences and neither do claims 1 or 2. Even with respect to the expressed sequences of claim 3, it is unclear if the limitation of claim 19 is directed to part (a) or (b) or both.

Claim 21 is confusing in reciting "said at least one sequence." This claim depends upon claim 8 which in turn depends upon claims 1, 2, or 3. Claim 8 does not recite "at least one sequence." Claims 1, 2, and 3 recite "at least one sequence" with respect to computational means (database comparison) and not experimental means (subtractive hybridization).

Claim 52 appears to contain all of the limitations of claim 51 as claim 50 already requires that the sequences are expressed sequences. Alternatively, claim 51 provides no steps to distinguish expressed from non-expressed sequences in the library.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

~~Claims 1 and 3 The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:~~

~~A person shall be entitled to a patent unless –~~

Claims 1, 3-6, 50-53, and 58-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Sabatini et al. (U.S. Patent No. 5,966,712).

Sabatini et al. discloses making nucleic acid libraries from various host organisms, obtaining sequence information therefrom (including expressed sequences), and searching other databases to determine unique or common sequences. Computational subtractions and Southerns are disclosed (See abstract, claims, at least columns 1-3, Example 1, and Figures.) Microbial libraries (including symbiotic and pathogenic) are specifically disclosed. Note that although the preamble of the claims is directed to identifying a microbe, the method steps only require obtaining sequence information and searching a database to determine presence or absence of sequences. The computer system and method of Sabatini et al. perform these steps.

Claim 58 is rejected under 35 U.S.C. 102(b) as being anticipated by Fredericks et al.

Fredericks et al. took a sample of CSF to provide DNA from a human patient. The DNA was amplified using PCR and the amplified sequences compared to a database of known microbial 16S rRNA to identify the microbe. (See pages 475-476.)

Conclusion

The art to Meyerson, Weber, and Relman made of record is considered pertinent to applicant's disclosure. This art is not prior to the instant application.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 703-308-0666. The examiner can normally be reached on Monday-Friday, 8:30 am - 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Marianne P. Allen
Primary Examiner
Art Unit 1631

mpa
February 7, 2003